

# REPLACEMENT SHEET

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Sheet 1 of 1

Title: RATIONAL EVOLUTION OF CYTOKINES FOR HIGHER STABILITY,

THE CYTOKINES AND ENCODING NUCLEIC ACID MOLECULES

Applicants: Rene Gantier et al. Attorney Docket No. 17109-012001/922

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Cytokine regions susceptible to protease attack identified by structural alignment with Lead mutants

of IFN  $\alpha$ -2b

IFN- $\alpha$ 2b

CDLPOTHSLIGSRRTLMLLAQMRKISLFSCLKDQRHDFGGPQEEPGNQFQKAETIPVLUHEMIOQIFNLESTKDSSAAWDETLLDKFTYELYQQLNDLEACVIQG

VGVTETPLMREDISILAVRKYFORITLYKEKKYSPCAEVURAEIMRSFSLSTNLQESLRKE

Exemplary protein of the interferons/interleukin-10 family

IFN- $\beta$

MSYNLLGFLQRSSNFQCQKLLWQLINGRLEYCILKDRMNFDPIEEIKOLOQFOEDALITYEMLNQIFNTAIFRQDSSSTGWNETIVENILANVYHQINHLKTVLEEK

LEKEDFTRGKIMSSILHLKRYGRILHLYKAEYSHCANTIVRVEILRNFYFINRLTGYLRN

Exemplary protein of the short-chain cytokines family

EPO

APPRLCIDDSRVLERYLLEAKEAENTGCAEHCSLNENITVEDTKVNFYAWKRMEVGQQAVEVWQGLALLSEAVLRQOALLVNSSOPWEPLQLHVDKAVSGLRL

TLLRALGAKQEAISPPDAASAPPLRITTADFRKLFRVYSNFLRGKLLYTGEACRTGDR

Exemplary protein of the long-chain cytokines family

G-CSF

TPLGPASSLPLQSFLIKCLEQVRKIQGDAALQEKLVSECATVKLCHPEELVLIGHSIGIPWAPLSSCPSQLAGCLSQLHSGLPLYQGLQALEGISPELGPTLDLQL

DVADEATTIWQMEELGMAPAOPTCAMPAFASAFFORRAGCSVLASHLQSFLEVSYVLAQ

**FIG. 9**